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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/723,435
Filing Date: November 26, 2003
Appellant(s): XIONG ET AL.

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Field Code Changed

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DAVID W. OSBORNE
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed February 12, 2009 appealing from the Office action mailed September 28, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,352,715	Hwang et al.	3-2002
6,365,178	Venkateshwaran et al.	4-2002

(9) Grounds of Rejection

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 81-84, 86, 102, and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,352,715 ('715) with the effective filing date February 19, 1998 in view of US 6,365,178 ('178) with the effective filing date September 08, 1998.

US '715 teaches a transdermal drug delivery system to administer huperzine A in a controlled release skin patch designed for once-a-week application to treat Alzheimer disease (AD) (abstract; col.3, lines 55-65; col.4, lines 7-15; col.9, lines 1-7, 31). The patch comprises polyacrylate adhesive layer containing huperzine (col.9, lines 32-35; col.14, lines 65-67). The reference suggests the use of co-solvents to increase skin permeability of huperzine A (col.8, lines 65-67).

However, US '715 does not teach the blood plasma levels of huperzine provided by the transdermal system as instantly claimed.

The blood plasma levels are controlled by the amount of the drug included in the system as well as by the ingredients of the transdermal formulation used to deliver the huperzine such as the type of the adhesive, the permeation enhancers and other additives in the formulation.

Therefore, the claimed blood plasma levels of huperzine can be determined by one having ordinary skill in the art by manipulating the transdermal formulation containing the huperzine and the structure of the transdermal device delivering it. Additionally, individual patient-need is also a controlling factor in determination of the dose of huperzine.

It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller,* 105 USPQ 233.

US '175 does not explicitly teach the transdermal device comprises adhesive matrix and specific permeation enhancer as instantly claimed by claim 81.

US '178 teaches transdermal delivery device having adhesive matrix wherein the physical stability of the drug in the matrix is excellent and crystallization of the drug is inhibited (abstract). The adhesive matrix is suitable to deliver antiparkinsonism drugs and anticholinergic drugs (col.6, lines 18-20). The adhesive matrix comprises acrylic or rubber adhesives and permeation enhancer including fatty acid esters including lauryl lactate (col.6, line 42; col.7, lines 45-65; col.22, lines 36-38).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD wherein the system comprises polyacrylate adhesive and may contain permeation enhancer as disclosed by US '715, and provide huperzine in adhesive matrix comprising permeation enhancer including fatty acid ester of lactic acid as disclosed by US '178 because US '715 disclosed huperzine as being capable to be provided combined with acrylic materials and enhancers and because US '178 teaches polyacrylate adhesive matrix comprising enhancers is suitable to deliver antiparkinsonism and anticholinergic drugs while such adhesive matrix shows excellent physical stability of the included drugs and inhibition of their crystallization, with reasonable expectation of having a transdermal delivery system to treat AD comprising huperzine in adhesive matrix comprising acrylate or rubber adhesive and fatty acid ester permeation enhancer wherein the matrix has excellent physical stability of the drug in the matrix without drug crystallization to provide the desired blood plasma levels of huperzine for extended time to treat the AD patients with great success.

(10) Response to Argument

Appellant's arguments filed 02/12/2009 have been fully considered but they are not persuasive.

Appellant argues that U.S. '715 teaches a transdermal drug delivery system to administer Huperzine A in a controlled release skin patch designed for once-a-week administration to treat Alzheimer disease (AD), however, U.S. '715 fails to teach the

claimed blood plasma levels of Huperzine or the transdermal device having an adhesive matrix and the claimed permeation enhancers. The Examiner attempts to cure the deficiencies by citing to U.S. '178 that is not drawn to any particular drug, but discloses numerous broad categories of drugs which could be included in matrix patch citing in excess of 40 different categories of drugs including the broad class antiparkinsonism drugs. U.S. '178 provides a broad and lengthy list of cell envelope disordering compounds or permeation enhancers. U.S. '178 provides limited teachings or correlation of specific active agents with specific permeation enhancers and provides no teaching correlating fatty acid esters of lauryl alcohol with antiparkinsonism drugs, let alone huperzine.

In response to these arguments, it is noted that appellants admits that U.S. '715 teaches a transdermal drug delivery system to administer Huperzine A in a controlled release skin patch designed for once-a-week administration to treat Alzheimer disease. Regarding the plasma level of huperzine, applicants' attention is directed to the fact that US '715 disclosed the amount of the drug used in the transdermal patch in acrylate adhesive is 1.5 to 2.25% (table 2), and applicants disclosed 1-20% huperzine in their formulations (examples). Therefore, US '715 teaches the same claimed adhesive, same drug in the same amount, and further teaches permeation enhancer. Hence one would expect the same plasma level is provided since the same components would be expected to yield the same plasma level. Further applicants disclosed in pages 21-23 that the claimed plasma level is achieved by permeation rate of huperzine to the skin between 0.01 to 15 $\mu g/cm^2/hr$, and the reference teaches effective permeation rate

more than 1.46 μg/cm^2/hr (claim 11 of the reference). It is expected the same delivery rate from similar formulation will provide the same plasma level. Therefore, those of ordinary skill in the art would have been readily optimized effective dosages and concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient. Determination of the appropriate dosage for treatment involving the above mentioned formulation would have been routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed prior art.

Additionally, in response to the argument that US '715 does not teach adhesive matrix, it is noticed that the reference teaches adhesive matrix at col.10, lines 15-30. Further, at col.12, lines 8-12, teaches that the drug is present in adhesive matrix. Adhesive matrix is therefore clearly taught by US '715.

Further, in response to the argument that US '715 does not teach permeation enhancer, it is pointed out that US '715 suggested permeation enhancers and stated at col.8, lines 65-67 that: "A reservoir formulation or using a combination of co-solvents to increase the skin permeability of neutral Hup A could be a viable approach." Therefore the reference suggested permeation enhancers as viable approach, and this would have suggested to one having ordinary skill in the art to add permeation enhancer to the transdermal patch comprising adhesive and delivering huperzine.

Regarding US '178, it is argued that the reference is relied upon for the solely teaching specific permeation enhancer as instantly claimed. US '715 already teaches

transdermal drug delivery system to deliver huperzine to treat patients suffering from AD as instantly claimed, wherein the system comprises polyacrylate adhesive and may contain permeation enhancer, and what is missing from the teaching of US '715 is the specific enhancer that is taught by US '178. US '178 show suitability of delivering drugs including antiparkinsonian drugs from acrylic adhesive with permeation enhancers wherein such combination of adhesive matrix with the enhancer shows excellent physical stability of the included drugs and inhibition of their crystallization. US '178 disclosed fatty acid ester of lactic acid included in the transdermal formulation for the same function as desired by appellant. US '178 teaches the functional equivalency of permeation enhancer of alcohol disclosed by US '715 and fatty acid esters of lactic acid, and teaches only two categories of enhancers classified as fatty acid esters and alcohols. Furthermore, appellant failed to show unexpected results obtained from the specific fatty acid esters of lactic acid, no factual stating of unexpected results. It has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 82 USPQ2d 1385, 1397 (2007).

Appellant argues that the Examiner has not expressly stated which obviousness rational she relies on, and it appears that the Examiner has applied the TSM test that some teaching, suggestion, or motivation in the prior art [including the references themselves and/or the knowledge generally available to one of ordinary skill in the art] that would have led one of ordinary skill in the art to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. In forming the above described combination, the Examiner has not relied on any teaching, suggestion, or motivation found in the cited references themselves to form the cited combination nor has the Examiner provided any finding that there was reasonable expectation of success. Rather the Examiner has relied on a broad and unsubstantiated assertion that the necessary teaching, suggestion, or motivation to combine the references teachings was in the knowledge generally available to one of ordinary skill in the art.

In response to this argument, it is argued that there is motivation to combine the cited references and expected success exists. US '715 teaches a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD wherein the system comprises polyacrylate adhesive and may contain permeation enhancer and further teaches the same adhesive and the same amount of the drug used by appellants, however US '715 does not teach specific enhancers. US '178 teaches polyacrylate adhesive matrix comprising enhancers that is suitable to deliver any pharmacologically active agent known for transdermal administration, and mentioned antiparkinsonism and anticholinergic drugs, wherein huperzine falls. US '178 further teaches that such adhesive matrix comprising acrylate adhesive and enhancer shows

excellent physical stability of the included drugs and inhibition of their crystallization. Therefore, at the time of the invention, one having ordinary skill in the art would have provided a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD wherein the system comprises polyacrylate adhesive matrix and may contain permeation enhancer as disclosed by US '715, and would have provided huperzine adhesive matrix comprising permeation enhancer including fatty acid ester of lactic acid as disclosed by US '178. One would have been motivated to do so because US '715 disclosed huperzine as being capable to be provided combined with acrylic materials and enhancers and because US '178 teaches polyacrylate adhesive matrix comprising enhancers is suitable to deliver any pharmacologically active agent known for transdermal administration, and suggested antiparkinsonism and anticholinergic drugs, and because US '178 teaches that such adhesive matrix shows excellent physical stability of the included drugs and inhibition of their crystallization. One would have reasonably expected formulating a transdermal delivery system to treat AD comprising huperzine in adhesive matrix comprising acrylate adhesive and fatty acid ester permeation enhancer wherein the matrix has excellent physical stability of the drug in the matrix without drug crystallization to provide the desired blood plasma levels of huperzine for extended time to treat the AD patients with great success. As such, there is motivation to combine US '715 and US '178 provided by both references. Furthermore, the examiner repeats that appellant failed to show unexpected results obtained from the specific fatty acid esters of lactic acid, no factual stating of unexpected results. Additionally, the examiner recognizes that obviousness can only be

established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

Appellant argues that transdermal drug delivery is a very complex and delicate art. For example, the identification of specific permeation or penetration enhancers for specific active agents is an extremely difficult and complicated challenge. The Appellants submit that such teachings regarding the fickle and unpredictable nature of penetration enhancers are generally known in the art. There are numerous examples of

third party teachings regarding the difficulty of formulating transdermal matrix patches, and in particular selecting and formulating with permeation enhancers, such as US 5,500,222, US 7,214,381, US 6,267,984.

In response to this argument, it is argued that the third party references all concern the interaction between the enhancers with polymers/adhesives. For example, US 5,500,222, col.3, lines 10-13, stated that "***permeation enhancer can cause among other problems, cohesive failure of adhesive***". The third party reference US 7,214,381 further teaches and suggests acrylic acid and lauryl alcohol enhancer as being suitable to different group of active agent as it stated that: "It has been discovered that in a transdermal formulation comprising ***different group of drugs*** as active agents; ***lauryl alcohol*** and diethylene glycol monoethyl ether as penetration enhancers, in a ternary vehicle composite comprised of ethanol, propylene glycol and purified water, using a ***polymer or copolymer of acrylic acid***, preferably a carbomer as gelling forming, provides therapeutically effective serum concentration of each active agent throughout at least a 24 hours period". Therefore, both the primary and secondary cited references teach acrylate adhesives and US '178 in example 11 teaches the combination of **acrylate adhesive and lauryl lactate without any interaction**. Therefore, instantly claimed acrylate adhesive is safe to be combined with fatty acid ester of lactic acid with no interaction as further evident by the third party reference US 7,214,381.

Appellant argues that the teachings regarding the difficulty of formulating transdermal systems and identifying permeation enhancers are ample evidence the knowledge of those of ordinary skill in the art. One of ordinary skill in the art would not have had reason to combine the cited references nor would they have had reasonable expectations of success in forming such a combination in a manner as required by the present claims. U.S. '715, provides additional evidence regarding the difficulty and unpredictability of formulating with permeation enhancers when it states: "[a] possible method to increase the concentration of undisassociated form of Hup A may be to add non-polar solvents such as alcohols and glycols. However, these agents also reduce partitioning of drugs into the skin. Thus various co-solvents need to be evaluated to achieve balance of satisfactory solubility and partitioning." Col. 8, lines 47-52.

In response to this argument, it is argued that US '718 teaches the combination of acrylic adhesive and the claimed enhancer and teaches that any drug suitable for transdermal administration can be delivered with this combination. Additionally, the third party reference "US 381" suggested the instant acrylic adhesive and permeation enhancer. US '715 suggested permeation enhancers and stated at col.8, lines 65-67 that: "A reservoir formulation or using a combination of co-solvents to increase the skin permeability of neutral Hup A could be a viable approach." Therefore the reference suggested permeation enhancers as viable approach, and this would have suggested to one having ordinary skill in the art to add permeation enhancer to the transdermal patch comprising adhesive and delivering huperzine. US '715 suggested and does not teach away from adding permeation enhancer. In considering the disclosure of the reference,

it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972). Furthermore, the examiner repeats that appellant failed to show unexpected results obtained from the specific fatty acid esters of lactic acid, no factual stating of unexpected results.

Appellant argues that the Examiner has not established a prima facie case of obviousness. The Examiner has not shown teaching, suggestion, or motivation found in either the references themselves to support the presently asserted combination, and no predictable success. Further, as set forth above, the Examiner's assertion that one of ordinary skill in the art would have been motivated and had a reasonable expectation success in arriving at the claimed invention based on the two cited references is inaccurate and clearly misconstrues the level of skill required in the art.

In response to this argument, it is argued that motivation to combine the references and reasonable expectation of success do exist and previously discussed as set forth in this examiner answer responding to absence of TSM. Further, a conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

Appellant argues that, although U.S. '178 sets forth a lengthy laundry list of possible permeation enhancers which can be used in the matrix patches, including the broad category of "saturated and unsaturated fatty acids and their esters, the only teaching of a fatty acid ester of lactic acid as a permeation enhancer is found in Example 11 that is drawn to specific transdermal formulations for diclofeanc, buspirone, and clonidine, each of which is in a distinct family of drugs far removed from Huperzine. Nothing in U.S. ' 178 correlates or connects the use of lactic acid esters, or any other permeation enhancer, with Huperzine or any other Anti-Parkinson drug.

In response to this argument, it is argued that US '178 does not teach laundry list of enhancer, rather it teaches finite number of categories of enhancers classified as fatty acid esters and alcohols. It has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is

motivation "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 82 USPQ2d 1385, 1397 (2007).

Additionally, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery system to deliver huperzine to treat patients suffering from AD wherein the system comprises polyacrylate adhesive and may contain permeation enhancer as disclosed by US '715, and provide huperzine in adhesive matrix comprising permeation enhancer including fatty acid ester of lactic acid as disclosed by US '178 because US '715 disclosed huperzine as being capable to be provided combined with acrylic materials and enhancers and because US '178 teaches polyacrylate adhesive matrix comprising enhancers is suitable to deliver any drug suitable for transdermal delivery including antiparkinsonism and anticholinergic drugs while such adhesive matrix shows excellent physical stability of the included drugs and

inhibition of their crystallization, with reasonable expectation of having a transdermal delivery system to treat AD comprising huperzine in adhesive matrix comprising acrylate or rubber adhesive and fatty acid ester permeation enhancer wherein the matrix has excellent physical stability of the drug in the matrix without drug crystallization to provide the desired blood plasma levels of huperzine for extended time to treat the AD patients with great success. US '178 recognized combination of acrylate adhesive with lauryl lactate without interaction and suggested any drug suitable for transdermal delivery, however exemplified NSAID. The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.*, 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

Appellant argues that reconstruction based upon hindsight reasoning is permissible only "so long as it takes into account only knowledge which was within the level of the ordinary skill at the time the claimed invention was made and does not include knowledge gleaned only from the applicant's disclosure...". Accordingly, the asserted combination of references is improper because it relies on impermissible hindsight. At the time of the present invention, and continuing through the present day, the knowledge of one of ordinary skill in the art was and is not sufficient to cause one of ordinary skill to have combined the teachings of the asserted references. Appellant argues that the Examiner has only arrived at the claimed invention from the cited references by using knowledge which was gleaned from the Appellants' disclosure.

In response to this argument, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The present invention, as previously discussed, is based on the teaching of the references and what was available to one having ordinary skill in the art at the time of the invention. The rejection also provided motivation, suggestion and teaching in the prior art to combine the reference to lead to the present invention. Additionally, a reasonable expectation of success provided by combination of the references, as set forth in this office action. These references (US '715 and US '178) show that it was well known in the art at the

time of the invention to use the claimed active ingredient huperzine treated AD when administered in transdermal formulation comprising acrylic polymer and permeation enhancer, however, does not teach specific enhancer that was taught by US '178 to be suitable to be combined with acrylic adhesive and any transdermally administrable drug. It is well known that it is prima facie obvious to combine two or more components each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Pinten,* 459 F.2d 1053, 173 USPQ 801 (CCPA1972); *In re Susi,* 58 CCPA 1074, 1079-80) 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crockett,* 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). No patentable invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients. See *In re Sussman*, 1943 C.D. 518; *In re Huellmantel* 139 USPQ 496; *In re Crockett* 126 USPQ 186.

Appellant argues that the Examiner has conceded that the presently claimed blood plasma levels of Huperzine are not taught by U.S. '715 or by U.S. '178, but continues to assert that such blood plasma levels could be readily determined by one having ordinary skill in the art and are inherently taught by U.S. '715. Appellant continues to dispute these assertions and argues that the cited references fail to teach the blood plasma level claim limitation because blood plasma levels are the key of the formulation design of transdermal delivery system, which is affected by numerous

factors including selection of proper adhesive, selection of proper permeation enhancers and their quantity, drug load, delivery rate, and depletion rate. Further, the present claims require specific blood plasma levels for a period of at least three days. The drug delivery rate alone is not determinative of blood plasma levels, but rather only one of a myriad of interconnected factors.

In response to this argument, it is repeated that US '715 disclosed the amount of the drug used in the transdermal patch in acrylate adhesive is 1.5 to 2.25% (table 2), and applicants disclosed 1-20% huperzine in their formulations (examples). Therefore US '715 teaches the same claimed adhesive, same drug in the same amount, and further teaches permeation enhancer. Hence, one would expect the same same plasma level would be provided since the same components would be expected to yield the same plasma level. Further applicants disclosed in pages 21-23 that the claimed plasma level is achieved by permeation rate of huperzine to the skin between 0.01 to 15 $\mu g/cm^2/hr$, and the reference teaches effective permeation rate more than 1.46 $\mu g/cm^2/hr$ (claim 11 of the reference). US '715 further teaches transdermal delivery of huperzine for the same period of time as instantly claimed. It is expected the same delivery rate from similar formulation will provide the same plasma level. A conclusion of obviousness does not require absolute predictability, only reasonable expectation of success, and references are not evaluated by their own disclosure, but what they would have suggested to one versed in the art. Those of ordinary skill in the art would have been readily optimized effective dosages and concurrent administration regimens as determined by good medical practice and the clinical condition of the individual patient.

Determination of the appropriate dosage for treatment involving the above mentioned formulation would have been routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information disclosed prior art.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Isis A Ghali/

Primary Examiner, Art Unit 1611

Conferees:

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611/Dave Nguyen/Dave Nguyen, QAS

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